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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,905	10/05/2005	Oliver Schadt	MERCK-3075	6249

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EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,905	SCHADT ET AL.	
	Examiner	Art Unit	
	Noble Jarrell	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/22/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. The rejection under 35 U.S.C. 102(a) has been overcome by the rejection.

2. The IDS submitted 5/23/2008 has been full considered.

3. As a result of the amended claims, claims 1-9 and 11-17 are being acted on in this action.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-9 and 11-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for enantiomers, mixtures of enantiomers, and racemates of compounds of formula I, does not reasonably provide enablement for solvates of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Vippagunta et al. (*Advanced Drug Delivery Reviews*, **2001**, *48*, 3-26) state that the formation of solvates or hydrates is unpredictable, even in a series of related of compounds, because each molecule has a unique shape (section 3.4, page 18). This rejection is maintained because applicants have not shown that their prepared compounds can actually form solvates.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a

single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of all the relevant factors to establish a *prima facie* case for lack of enablement is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to compounds of formula I, in which a pyrazole ring is directly connected to a substituted benzene ring.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Solvate formation is unpredictable. See Vippagunta et al. cited supra.

(5) The relative skill of those in the art:

One of ordinary skill in the art is a chemist familiar with the synthetic techniques in the specification.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for preparation of the enantiomers and racemates of formula I, but not the solvates of formula I.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 1-9 and 11-17 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

5. Claims 11-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of premenstrual syndrome, does not reasonably provide enablement for simultaneous treatment and prevention of disorders as well the treatment of all disorders associated with serotonin receptors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Applicants are enabled for treatment of premenstrual syndrome through 5-HT receptors. It is not possible to simultaneously treat and prevent a patient simultaneously. If a patient has a disease, it can only be treated. If a patient does not have a disease, it can only be prevented.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a method of treating and/or preventing disorders associated with 5-HT receptors with compounds comprising a pyrazole-phenyl or pyrazole-pyridine core.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Ross et al. (*Expert Opinion on Therapeutic Patents*, **2003**, *13(10)*, 1491-99) teach that treatment of premenstrual syndrome is viable through 5-HT receptors (section 3, pages 1494-95). This reference does not suggest the prevention of PMS.

(5) The relative skill of those in the art:

One of ordinary skill in the art is a scientist with a Ph. D.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for the treatment of premenstrual syndrome only.

However, the specification does not provide guidance for: prevention of conditions associated with 5-HT receptors, simultaneous treatment and prevention of any conditions associated with 5-HT receptors ; or treatment of all disorders associated with 5-HT receptors.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 11-16 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. What chemical groups does the variable "het" stand for in this claim? The term is not described by name, structure or function in claim 17. Claim 17 is incomplete.

8. Regarding claim 1, the phrase "in particular" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-4, 14, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhu et al. (US20020091116, published July 11, 2002). Zhu et al. teach examples 129, 130, and 141 (pages 197 and 200). In each of these compounds, variable R^2 is methyl (alkyl). In compounds 129 and 130, variable R^6 is phenyl and variable R^3 is C(O)NH-4-chloro-phenyl or C(O)NH-4-methoxy-phenyl. In compound 141, variable R^6 is C(NH)-pyrollidine (variable "het') and variable R^3 is C(O)NH-4-bromo-2-pyridyl (variable "het'). Compositions of these compounds are taught on page 163, paragraph 0897. This rejection is maintained because these compounds still anticipate the specified claims.

11. Claims 1-4, 7, 14, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Xiang et al. (WO 98031227, published July 23, 1998). Xiang et al. teach example 1, page 15, which anticipates formula IA of claim 7. Variable R^1 is CO_2Et, R^6 is 2-formyl-phenyl, and R^3 is $O(CH_2)_2$-Morpholine (variable "het'"). Compositions are taught on page 15, lines 3-32. This rejection is maintained because these compounds still anticipate the specified claims.

12. XP-002283830, submitted as part of the IDS, is considered prior art.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claims 1-4, 14, 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhu et al. (same reference as the 102(b) rejection). Zhu et al. teach compound 146 (page 201), which renders compounds of claim 17 obvious. In compound 146, variable R^4 is methyl (alkyl), R^3 is C(O)NH-4-bromo-2-pyridyl (variable "het'"), and R^6 is C(NH)-4-methyl-piperazine (variable "het'). The motivation for preparing this compound arises from its use as a cannabinoid receptor modulator. This rejection is maintained because these compounds still anticipate the specified claims.

Claim Objections

16. Claim 17 is objected to because of the following informalities: it does not end with a period. Appropriate correction is required.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-7, 14, 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4-17 of copending Application No. 10/552064. Although the conflicting claims are not identical, they are not patentably distinct from each other because compound 479 (page 37, second column) of application 10/551905 can be embraced by the specified claims in both applications. This rejection is maintained because one or more compounds that are encompassed by claims in both applications.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

2. Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/552065. Although the conflicting claims are not identical, they are not patentably distinct from each other because overlapping subject material is shared between these claims. Compound 440 (page 63) of application 10/552065 is encompassed by the specified claims in both applications. This

rejection is maintained because one or more compounds that are encompassed by claims in both applications.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

19. No claims are allowed.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624